

What is claimed is:

1. A method of determining whether a subject is at increased risk for alcoholism, said method comprising:

(a) administering to a subject a therapeutically effective amount of a GABA_A receptor modulator and determining whether the subject is sensitive or insensitive to such GABA_A receptor modulator;

(b) subsequently administering a therapeutically effective amount of a GABA_A receptor agonist and determining whether the subject is sensitive or insensitive to such GABA_A agonist; and

(c) correlating a decreased sensitivity to a GABA_A receptor modulator and an increased sensitivity to a GABA_A agonist with an increased risk of alcoholism in the subject.

2. The method of claim 1 wherein the GABA_A receptor modulator is a benzodiazepine.

3. The method of claim 1 wherein the GABA_A receptor agonist is gaboxadol or THIP.

4. The method of claim 2 wherein the benzodiazepine is Valium (diazepam), Activan (lorazepam), Midazolam, or Flunitrazepam.

5. The method of claim 4 wherein the dose range is from about 5 to about 20 mg.

6. The method of claim 3 wherein the dose range is from about 1 to about 3 mg/kg.

1181-19 PCT

7. A method of screening for a drug which decreases expression of the $\alpha\beta_2\delta$ subunit of GABA_A, said method comprising:

- (a) isolating and culturing neurons;
- (b) applying a drug to the cultured neurons;
- (c) measuring the level of δ subunit of GABA_A from the treated neurons of step (b);
- (d) determining whether the drug applied in step (b) decreases expression of the δ subunit of GABA_A receptors; and
- (e) correlating a decrease in expression of the δ subunit of GABA_A receptors found in the treated neurons of step (b) when compared to a control neuron culture having no drug application, with the identification of a drug which decreases expression of $\alpha_4\beta_2\delta$ GABA_A receptors.

8 A method of screening for a drug which decreases expression of the $\alpha_4\beta_2\delta$ subunit of GABA_A receptor, said method comprising: (a) expressing $\alpha_4\beta_2\delta$ GABA_A receptors in eukaryotic cells; (b) applying a drug to the eukaryotic cells of (a); (c) measuring the level of δ subunit of GABA_A from the treated eukaryotic cells of step (b); (d) determining whether the drug applied in step (b) decreases expression of the δ subunit of GABA_A receptors; and (e) correlating a decrease in expression of the δ subunit of GABA_A receptors found in the treated eukaryotic cells of step (b) when compared to a control eukaryotic cell population having no drug application, with the identification of a drug which decreases expression of $\alpha_4\beta_2\delta$ GABA_A receptors.

9 A drug that decreases expression of the $\alpha_4\beta_2\delta$ subunit of GABA_A and identified by the method of claim 7 or 8.

10. A method of treating a subject at risk for alcoholism, said method comprising administering a therapeutically effective amount of a drug of claim 7, 8, or 9.

11. A method for identifying a drug which blocks $\alpha_4\beta_2\delta$ GABA_A receptors, said method comprising:

- (a) isolating and culturing neurons;
- (b) applying a drug to the cultured neurons of (a);
- (c) measuring GABA_A gated currents at $\alpha_4\beta_2\delta$ GABA_A receptors in the treated neurons of (b); and
- (d) correlating a decrease in GABA_A-gated currents recorded at $\alpha_4\beta_2\delta$ GABA_A receptors when compared to a control culture with no drug application, with the identification of a drug which blocks $\alpha_4\beta_2\delta$ GABA_A receptors.

12. A method for identifying a drug which blocks $\alpha_4\beta_2\delta$ GABA_A receptors, said method comprising (a) expressing $\alpha_4\beta_2\delta$ GABA_A receptors in eukaryotic cells ; (b) applying a drug to the eukaryotic cells of (a); (c) measuring GABA_A gated currents at $\alpha_4\beta_2\delta$ GABA_A receptors in the treated eukaryotic cells of (b); and (d) correlating a decrease in GABA_A-gated currents recorded at $\alpha_4\beta_2\delta$ GABA_A receptors when compared to a eukaryotic cell population having no drug application, with the identification of a drug which blocks $\alpha_4\beta_2\delta$ GABA_A receptors.

13. A drug which blocks $\alpha_4\beta_2\delta$ GABA_A receptors and identified by the method of claim 10, 11, or 12.

14. A method of treating a patient at risk for alcoholism, said method comprising administering a therapeutically effective amount of the drug of claim 11, 12 or 13.

15. A method of determining whether a subject is at increased risk for premenstrual anxiety, said method comprising:

(a) administering to a subject a therapeutically effective amount of a GABA_A receptor modulator and determining whether the subject is sensitive or insensitive to such GABA_A receptor modulator;

(b) subsequently administering a therapeutically effective amount of a GABA_A receptor agonist and determining whether the subject is sensitive or insensitive to such GABA_A agonist; and

(c) correlating a decreased sensitivity to a GABA_A receptor modulator and an increased sensitivity to a GABA_A agonist with an increased risk of premenstrual anxiety in the subject.

16. The method of claim 15 wherein the GABA_A receptor modulator is a benzodiazepine.

17. The method of claim 15 wherein the GABA_A receptor agonist is gaboxadol or THIP.

18. The method of claim 16 wherein the benzodiazepine is Valium (diazepam), Activan (lorazepam), Midazolam, or Flunitrazepam.

19. The method of claim 18 wherein the dose range is about 5-20 mg.

20. The method of claim 17 wherein the dose range is about 1-3 mg/kg.

21. A method of treating a subject at risk for premenstrual anxiety, said method comprising administering a therapeutically effective amount of a drug of claim 7, 8, or 9.

22. A drug which blocks $\alpha_4\beta_2\delta$ GABA_A receptors and identified by the method of claim 11, 12 or 21.

1181-19 PCT

23. A method of treating a patient at risk for premenstrual anxiety, said method comprising administering a therapeutically effective amount of the drug of claim 11, 12 or 13.

24. The method of claim 8 or 12 wherein the eukaryotic cells are *Xenopus laevis* oocytes, Chinese hamster ovary (CHO) cells, mouse fibroblast L929 cells, mouse L(-tk) fibroblast cell line, human embryonic kidney cells, green monkey kidney cells, or COS cells.